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DOCUMENT-IDENTIFIER: US 20030059944 A1

TITLE: Method for expression of small antiviral RNA molecules within a cell

Detail Description Paragraph (98):

[0142] In one embodiment of the invention, the retroviral construct has an RNA coding region that encodes a double stranded molecule having at least 90% homology to the HIV viral RNA genome, an expressed region of the HIV viral genome, for example, to any region of about 19-25 nucleotides in length of the 9-kb transcript of the integrated HIV virus, or any of the variously spliced mRNA transcripts of HIV (Schwartz, S; Felber, B K; Benko, D M; Fenya, E M; Pavlakis, G N. Cloning and functional analysis of multiply spliced mRNA species of human immunodeficiency virus type 1. J. Virol. 1990; 64(6): 2519-29). Target regions within the HIV transcripts can be chosen to correspond to any of the viral genes, including, for example, HIV-1 LTR, vif, nef; and rev. In another embodiment, the RNA coding region encodes a double stranded region having at least 90% homology to a receptor or co-receptor of the HIV virus. For example, the primary receptor for HIV entry into T cells is CD4. In a preferred embodiment, the co-receptors CXC chemokine receptor 4 (CXCR4) and CC chemokine receptor 5 (CCR5) are down-regulated according to the methods of the invention. CXCR4 (Fedderspiel et al. Genomics 16:707-712 (1993)) is the major co-receptor for T cell trophic strains of HIV while CCR5 (Mummidi et al. J. Biol. Chem. 272:30662-30671 (1997)) is the major co-receptor for macrophage trophic strains of HIV. Other cellular targets against HIV include the RNA transcripts for proteins involved in the HIV life cycle, including cyclophilin, CRM-1, importin-.beta., HP68 (Zimmerman C, et al. Identification of a host protein essential for assembly of immature HIV-1 capsids. Nature 415 (6867): 88-92 (2002)) and other as yet unknown cellular factors.